

# Neonatal Hyperviscosity Syndrome

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THE HYPERVISCOSITY SYNDROME is a symptom complex associated with decreased blood fluidity, which is generally associated with an increase in erythrocyte mass. The mean cord blood hematocrit is  $45 \pm 5\%$  and  $50 \pm 5\%$  in preterm and term infants respectively if they are born at sea level. Values are somewhat higher in infants born in locations at higher altitudes. A central venous hematocrit of 65% or more is generally accepted as the definition of polycythemia.

Although polycythemia may be associated with hyperviscosity of the blood, the two conditions are not synonymous, as not all hyperviscous infants are polycythemic nor are all polycythemic neonates hyperviscous.

The viscosity of a fluid is defined as the ratio of shear stress to shear rate. Shearing occurs as the result of internal friction of the fluid layers moving over one another during flow. It can be measured with a cone plate viscometer (such as a Wells-Brookfield Micro-Viscometer) over a range of shear rates. Two commonly used shear rates for blood are 11 and 106 seconds<sup>-1</sup>. These shear rates presumably approximate those in small venules and large arteries respectively. In several studies a direct curvilinear relationship has been found between hematocrit and blood viscosity, with viscosity increasing substantially at a hematocrit of more than 70%.

In contrast to Newtonian fluids, blood contains several factors that influence its viscosity:

- Cellular elements, erythrocytes, leukocytes and platelets. More recently the lack of erythrocyte deformability has been found to be an important factor.
- Plasma elements such as proteins, chylomicrons, electrolytes and water molecules.
  - Velocity of flow.
  - Suspension stability.

In addition, in narrower blood vessels the viscosity of blood depends more on the viscosity of plasma because the cells will gather in the faster axial zone, causing in effect a fall in hematocrit and blood viscosity (Fahraeus phenomenon). Because the plasma protein content is lower in neonates, this Fahraeus effect favors blood flow; however, sick neonates or infants of diabetic mothers may have macropoteins that can increase plasma viscosity.

Clinically the factors associated with increased incidence of hyperviscosity syndrome include

- Intrauterine hypoxia
- Intrauterine infection
- Developmental factors
  - Infants of diabetic or gestational diabetic mothers
  - Down's syndrome
  - Trisomy D
  - Adrenal hyperplasia
  - Oligohydramnios
- Placental dysfunction
  - Small for gestational age
  - Postmaturity
- Transfusion
  - Placental-cord
  - Twin-twin
  - Maternal-fetal
- Cyanotic congestion
  - Heart disease

Hyperviscosity may lead to sludging of blood flow with resultant impairment of tissue oxygenation and a tendency to form microthrombi. Impaired circulation and tissue hypoxia will result in the following disturbances: brain—central nervous system signs of irritability, jitteriness and convulsions, which may be associated with neurologic sequelae; heart—a fall in systemic cardiac output due to decreased venous return, an increased viscous load for the heart to pump and increased ratio of the right preejection period to right ventricular ejection time (RPEP/RVET); lungs—increased pulmonary vascular resistance leading to increased intrapulmonary shunting and poor gas exchange, producing symptoms such as cyanosis, tachypnea and cardiomegaly; kidneys—oliguria and hypoxic damage of glomeruli and tubules leading to proteinuria, hematuria, disturbances in sodium absorption and renal vein thrombosis; gastrointestinal tract—ischemia of bowel wall and necrotizing enterocolitis; blood—hypoxia, acidosis and hypoglycemia causing decreased erythrocyte deformability; thrombocytopenia, burr or fragmented cells and decreased blood flow, especially in the periphery; jaundice—probably due to breakdown of an increased number of damaged erythrocytes; hypoglycemia—nonnucleated erythrocytes have very little intracellular glycogen and therefore depend on serum glucose for their metabolism, and an increased number of erythrocytes may lead to greater glucose use. This may be an added etiologic factor in addition to tissue demands for glucose.

In addition to the underlying condition—such as small size for gestational age—the symptoms and signs associated with the condition include plethora, cyanosis, tachypnea, cardiomegaly, hypoglycemia, hypocalcemia, hypomagnesemia, hyperbilirubinemia, lethargy, poor feeding, jitteriness, seizures and oliguria.

Controversy exists as to when exchange transfusion, with either fresh frozen plasma or 5% salt-poor albumin solution, is warranted. This is largely because of

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the inconsistent correlation between the presence of clinical symptoms and signs with polycythemia or in vitro measurements of blood viscosity. However, in view of the potential dangers of hyperviscosity and findings that document abatement of clinical symptoms and signs following exchange transfusion, it would appear reasonable to do a partial exchange transfusion when an infant's central hematocrit is greater than 70% or viscosity is greater than 22 centipoise at 37°C at a shear rate of 11 seconds<sup>-1</sup>, or at lower central hematocrits (such as 63% to 70%) when they are associated with symptoms. The formula that can be used for calculating for an exchange transfusion is

$$\text{Volume of blood exchanged} = \frac{\text{blood volume} \times (\text{observed Hct} - \text{desired Hct})}{\text{observed Hct}}$$

where blood volume (neonatal) = 80 to 100 ml per kg of body weight and desired hematocrit (Hct) = 50% to 55%. Because fresh frozen plasma is a source of fibrinogen that can increase erythrocyte aggregation and thereby increase blood viscosity, 5% salt-poor albumin is the preferred solution used for partial exchanges.

Another simple way of calculating the exchange volume is to use 10% of an infant's estimated blood volume. Serial central hematocrits should be determined every three hours until the hematocrit is stable. A repeat exchange may sometimes be necessary. Some

authorities have advocated that the blood volume in these infants be reduced by 10 ml per kg of body weight at the end of a partial exchange transfusion. In view of the fact, however, that newborn infants with polycythemia can be hypovolemic, normovolemic or hypervolemic, this recommendation is not generally accepted.

Available follow-up data suggest that neurologic and developmental abnormalities are more common among infants who have polycythemia. The efficacy of partial exchange transfusion in preventing neonatal complications or reducing neurologic and developmental sequelae is controversial. One reason may be that sludging, microthrombi and pathologic changes may have occurred in utero. Another reason may be that the abnormal sequelae are the result of some underlying pathologic condition. Despite more intense focus on this clinical entity in recent years, more studies are necessary to better define the pathophysiology of the hyperviscosity syndrome.

#### GENERAL REFERENCES

- Black VD, Lubchenco LO, Luckey DW, et al: Developmental and neurologic sequelae of neonatal hyperviscosity syndrome. *Pediatrics* 1982 Apr; 69:426-431
- Brans YW, Shannon DL, Ramamurthy RS: Neonatal polycythemia: II. Plasma, blood and red cell volume estimates in relation to hematocrit levels and quality of intrauterine growth. *Pediatrics* 1981 Aug; 68:175-182
- Linderkamp O, Meiselman HJ, Wu PYK, et al: Blood and plasma viscosity and optimal hematocrit in the normal newborn infant. *Clin Hemorheol* 1981; 1:575-584
- Ramamurthy RS, Brans YW: Neonatal polycythemia: I. Criteria for diagnosis and treatment. *Pediatrics* 1981 Aug; 68:168-174